

## INTRODUCTION

### Digestive Diseases: Overview and Public Health Burden

The digestive system is a complex, multi-organ structure that performs many vital functions, including nutrient absorption and waste disposal. The tubular gastrointestinal (GI) tract includes the mouth, esophagus, stomach, small intestine, colon or large intestine, rectum, and anus. The luminal surface along much of this tract is lined with cells that either secrete substances that aid in breaking down ingested food or that absorb nutrients and water into the bloodstream for distribution throughout the body. The layers of muscles and associated nerves that surround the lumen propel food and waste through the system for eventual elimination. Even in healthy individuals, the digestive tract is colonized by thousands of microbial species that play a role in normal digestion and help maintain proper nutrition. Solid organs of the abdominal cavity also contribute to the digestive process. The pancreas secretes enzymes into the small intestine to help break down proteins, fat, and carbohydrates. The liver and biliary system (bile ducts, gallbladder) secrete bile into the small intestine to aid in the digestion of fat. In addition, the liver processes nutrients absorbed by the small intestine into forms that can be used by the body and detoxifies potentially harmful substances.

Diseases of the digestive system comprise an exceptionally diverse array of disorders and conditions. Conditions such as acute pancreatitis, appendicitis, and foodborne gastrointestinal infections develop suddenly and usually resolve in a relatively short time. Other disorders, including inflammatory bowel diseases and non-alcoholic steatohepatitis, are chronic and may be controlled, but not yet cured. Dysregulation of the immune system or inflammation can lead to celiac disease, Crohn's disease, eosinophilic esophagitis, or related conditions. Similarly, disorders such as Hirschsprung's disease, irritable bowel syndrome, and intestinal pseudoobstruction are associated with dysfunction of the nervous system or musculature of the GI tract. Digestive diseases can be caused by infectious agents, such as viral hepatitis or ulcers due to infection with *Helicobacter pylori*, or may be treatment-related, such as radiation proctitis, short bowel syndrome due to surgical resection of the gut, or ulcers caused by the use of non-steroidal anti-inflammatory drugs (NSAIDs). Cancer can develop along any part of the luminal gut or in the solid organs of the digestive system. Conditions named in this section are only a few examples of the many diseases that impact the digestive system.

The burden of digestive diseases on the U.S. healthcare system is substantial. At least 60 to 70 million Americans are affected each year by digestive diseases at a cost that exceeds \$100 billion in direct medical costs. Annually, about 14 million hospitalizations—10 percent of the total—and 15 percent of all in-patient hospital procedures are attributed to treatment for digestive diseases. In addition, 105 million visits to doctors' offices occur each year for digestive diseases, frequently in response to symptoms such as abdominal pain, diarrhea, vomiting, or nausea. Prescription drugs for the treatment of certain digestive diseases such as gastroesophageal reflux disease rank among the most commonly used pharmaceutical drugs in the U.S.

On a personal level, digestive diseases are associated with significant mortality, morbidity, and loss of quality of life. Digestive diseases, including cancer, are named as a primary cause of death for approximately 236,000 people in the U.S. each year. Moreover, digestive diseases can severely affect patients' quality of life and cause significant disability even for conditions that are not immediately life-threatening. Debilitating symptoms—such as chronic pain, discomfort, bloating, diarrhea, constipation, incontinence, social stigma, or embarrassment—that are associated with many GI disorders can impact patients' ability to work or engage in everyday activities. Collectively, these diseases account for over \$44 billion in indirect costs associated with disability and mortality each year.

Although digestive diseases in general can affect individuals of any age, race or ethnicity, gender, or socioeconomic status, some diseases disproportionately affect certain populations. For example, necrotizing enterocolitis occurs only in newborns, while diverticular disease is most frequently diagnosed in the elderly. The rate of some infectious GI diseases such as *H. pylori* and hepatitis B—both of which increase the risk of digestive cancers—is substantially higher among certain groups that emigrate from areas where these diseases are endemic, such as parts of Asia. Autoimmune diseases like celiac disease and inflammatory bowel diseases are more common in women. African Americans have a higher incidence of pancreatic cancer than any other racial/ethnic group in the U.S. and have a poorer prognosis at diagnosis. These and other significant health disparities provide both opportunities and challenges for research to reduce the public health burden of digestive diseases.

## **NIH-Supported Digestive Diseases Research**

### **Advances and Opportunities**

Decades of research in digestive diseases have significantly contributed to a reduction in the burden of many of these diseases on individual and public health. The cumulative efforts of scientists working to uncover the fundamental principles of digestive health and disease have been translated into clinical settings to develop and validate new disease-screening protocols, effective prevention strategies, including vaccines, and innovative behavioral, pharmacological, and surgical treatments.

The incidence of acute hepatitis B has plummeted in the U.S. due in part to the introduction of a vaccine to the virus that causes this disease. The development of tests that detect the presence of hepatitis B and C viruses in blood has nearly eliminated their transmission through blood donation, further reducing the public health threat of viral hepatitis. Likewise, the annual number of deaths from colorectal cancer has been declining in recent years. This decrease may be partially attributable to the availability of cost-effective screening techniques that improve the likelihood of detecting the disease at an early stage when it is more responsive to treatment. Research on inflammatory bowel diseases (IBD) supported the development of biologically based therapies, including multiple monoclonal antibodies directed against tumor necrosis factor (TNF), that have provided relief for many IBD patients who did not respond to other treatments. Finally, the discovery that ulcers can be caused by *H. pylori* infection quickly led to the realization that many ulcer patients can be cured by antibiotics.

These and other advances have truly revolutionized the care of many digestive disease patients or those who are at risk for developing digestive diseases. However, the burden of digestive diseases in the U.S. remains significant, and the sheer number and variety of these illnesses highlight the crucial need for ongoing attention to these diseases through a vigorous research effort. For example, very little is known about the causes of functional GI disorders, and individuals affected by these conditions have few treatment options. Likewise, patients with chronic pancreatitis often experience severe pain that is difficult to treat and can substantially reduce quality of life. Cancer of the digestive system remains an important cause of cancer-related death in the U.S. For these patients and the millions of other Americans afflicted with acute or chronic digestive diseases, the National Commission on Digestive Diseases sought to identify the most critical needs and promising opportunities in digestive diseases research that have the potential, if pursued, to advance the understanding of all forms of digestive diseases and alleviate the burden of these diseases.

## Digestive Diseases Research Funding

Progress in digestive diseases research has benefited from strong support from the National Institutes of Health (NIH) in recent years. Twenty NIH Institutes, Centers, and Offices currently support digestive diseases research on a variety of topics with a total expenditure of more than \$1.2 billion in fiscal year 2007 (Table 1).

The NIH research portfolio includes funding for studies of fundamental mechanisms of digestive system development and function, as well as basic, translational, and clinical research on the digestive system in normal states and disease conditions. NIH research is funded through grants, awards, contracts, and fellowships to extramural researchers and institutions for research and training, as well as support for intramural laboratories. To aid in the development of this long-range research plan, lists of grants and other awards comprising the NIH portfolio for digestive diseases were provided to members of the Commission and to each working group.<sup>1</sup>

**Table 1: NIH Expenditures for Digestive Diseases Research FY 2007 (in dollars)**

<b>NIH Institute, Center, Office or Fund*</b>	<b>FY 2007</b>
NCI	395,479,000
NIDDK	331,021,000
NIAID	273,792,000
NIDCR	83,650,000
NIEHS	32,865,000
NCRR	26,481,000
NIAAA	24,124,000
NHLBI	15,477,000
NICHD	14,705,000
NINDS	9,446,000
NCCAM	9,253,000
ROADMAP	8,014,000
NINR	2,638,000
NIA	1,900,000
FIC	1,234,000
NIDA	1,055,000
OD	910,000
NIBIB	794,000
NIMH	550,000
NHGRI	506,000
NCMHD	194,000
<b>TOTAL NIH</b>	<b>1,234,088,000</b>

\*See text for full titles of acronyms.

<sup>1</sup> Table 1 provides the most recent NIH funding data (FY 2007) as of the completion of this research plan in spring 2008. The Commission's charter required a scientific overview of NIH-funded research and research-related activities. In response to that mandate, the Commission and its working groups were provided with the most recently available aggregate funding data and lists of digestive diseases-related NIH research awards during the course of their discussions and development of research goals, which took place in 2006-2007. The FY 2006 award list used by the Commission will be made available on the Commission's website at <http://NCDD.niddk.nih.gov>

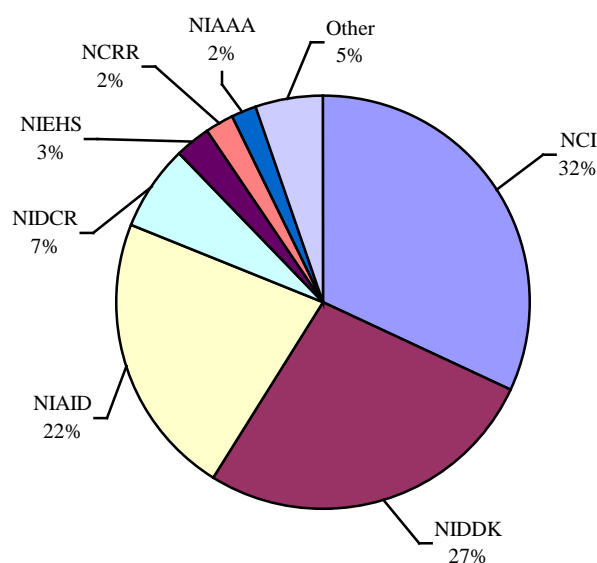
Institutes and Centers accounting for the majority of the NIH portfolio for digestive diseases research and research training (Figure 1) include:

- National Cancer Institute (NCI, 32 percent)
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK, 27 percent)
- National Institute of Allergy and Infectious Diseases (NIAID, 22 percent)
- National Institute of Dental and Craniofacial Research (NIDCR, 7 percent)
- National Institute of Environmental Health Sciences (NIEHS, 3 percent)
- National Center for Research Resources (NCRR, 2 percent)
- National Institute on Alcohol Abuse and Alcoholism (NIAAA, 2 percent)

Other NIH Institutes, Centers, and Offices that support digestive diseases research and research training include:

- National Heart, Lung, and Blood Institute (NHLBI)
- *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)
- National Institute of Neurological Disorders and Stroke (NINDS)
- National Center for Complementary and Alternative Medicine (NCCAM)
- NIH Roadmap for Medical Research (ROADMAP)
- National Institute of Nursing Research (NINR)
- National Institute on Aging (NIA)
- Fogarty International Center (FIC)
- National Institute on Drug Abuse (NIDA)
- NIH Office of the Director (OD)
- National Institute of Biomedical Imaging and Bioengineering (NIBIB)
- National Institute of Mental Health (NIMH)
- National Human Genome Research Institute (NHGRI)
- National Center on Minority Health and Health Disparities (NCMHD)

**Figure 1: NIH Awards for Digestive Diseases Research by Institute or Center**



## **Coordination and Communication of Digestive Diseases Research**

In addition to its direct role in funding digestive diseases research, the NIH engages in significant efforts to coordinate research programs within the agency and with other Federal agencies that share a common interest in combating digestive diseases. The Digestive Diseases Interagency Coordinating Committee (DDICC) is the primary mechanism for Federal digestive diseases research coordination. The DDICC brings together representatives from multiple NIH Institutes and Centers that fund digestive diseases research, as well as from other agencies, including the Agency for Healthcare Research and Quality, the Food and Drug Administration, the Department of Defense, the Centers for Disease Control and Prevention, the Department of Veterans Affairs, the Health Resources and Services Administration, and the Department of Agriculture, to discuss and coordinate digestive diseases-related research activities across the Federal government. The Liver Disease Subcommittee of the DDICC coordinates liver and biliary diseases research across the NIH and other Federal agencies, including efforts to implement the trans-NIH *Action Plan for Liver Disease Research*.

The NIH also promotes communication and collaboration within the digestive diseases research community through the support of conferences and workshops. For example, the NIH convened a state-of-the-science conference on prevention of fecal and urinary incontinence in adults to assess the scientific evidence relevant to understanding the epidemiology, risk factors, burden of illness, prevention strategies, and research priorities for these serious medical conditions. Other conferences have focused on diverse topics relevant to digestive diseases, including gastrointestinal microbiota and pre/probiotics research; nuclear receptors in liver and digestive disease; improving long-term outcomes for pediatric liver transplantation; acute liver failure; alcohol, intestinal bacterial growth, intestinal permeability to endotoxin, and medical consequences; screening and outcomes in biliary atresia; and management of hepatitis B. Many of these conferences and workshops are jointly sponsored by multiple NIH Institutes and Centers, other Federal agencies, and private professional or patient advocacy organizations.

The National Digestive Diseases Information Clearinghouse<sup>2</sup> was established by NIDDK in 1980 to increase knowledge and understanding about digestive diseases among people with these conditions and their families, healthcare professionals, and the general public. This service includes distribution of public information materials on a variety of digestive diseases, referrals to health professionals, and a reference collection on health education publications.

## **Genesis of the National Commission on Digestive Diseases and Its Long-Range Research Plan for Digestive Diseases**

### **Charter for the National Commission on Digestive Diseases**

Elias A. Zerhouni, M.D., Director of the National Institutes of Health, chartered the National Commission on Digestive Diseases on July 26, 2005, based on a mutual interest in advancing digestive diseases research shared by the NIH and the Congress. The establishment of the Commission responds, in part, to congressional report language accompanying the FY 2005 appropriations bills in the House and Senate for the Departments of Labor, Health and Human Services, and Education, and Related Agencies. The Commission was charged with two main tasks: (1) to conduct an overview of the state of the science in digestive diseases research exclusive of diseases of the oral cavity, and (2) to develop a 10-year plan for digestive diseases research that is consistent with the NIH mission and aimed at the ultimate goal of improving the health of the Nation through research. The Commission's primary focus has been to

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<sup>2</sup> The National Digestive Diseases Information Clearinghouse is accessible online at: <http://digestive.niddk.nih.gov/>.

identify compelling research opportunities that, if pursued, would improve the lives and health of individuals affected by digestive diseases.

The long-range research plan developed by the Commission, entitled *Opportunities and Challenges in Digestive Diseases Research: Recommendations of the National Commission on Digestive Diseases*, will serve as an important guide to help define NIH priorities for digestive diseases research over the next decade. Thus, the plan encompasses many broad areas of digestive diseases research that are relevant to the NIH mission, including fundamental biology of the digestive system and disease-oriented research topics such as epidemiology; environmental factors; genetics; mechanisms; diagnosis; causes; treatments; behavioral, social, and psychological factors; health disparities; prevention; and cures. Opportunities identified by the Commission span basic, translational, and clinical research, including clinical trials in children, adults, and in special populations such as high-risk groups or the disadvantaged. The plan also addresses issues related to research training and education of investigators in digestive diseases research fields. Finally, this research plan identifies challenges to its optimal implementation and proposes cross-cutting, innovative disciplines, technologies, and resources that would create research synergies and promote progress in digestive diseases research.

## **Development and Organization of the Commission**

### *Appointment of Commission Members and Formation of Working Groups*

The NIH Director appointed 16 Commission members who included extramural researchers from academic institutions across the country, medical professionals, and patient advocates (Appendix 2). These members were selected from more than 100 names submitted through a nomination process that was open to the entire research community and the general public. In addition, 22 *ex officio* members representing NIH Institutes and Centers, as well as other Federal agencies with an interest in digestive diseases research, served on the Commission (Appendix 2). The Commission was chaired by Stephen P. James, M.D., Director of the Division of Digestive Diseases and Nutrition of the NIDDK, which is the lead entity for coordination of digestive diseases research at NIH.

Shortly after the Commission's establishment, the members created "working groups" of additional external experts to provide input to the Commission for developing the individual chapters of the research plan. Therefore, a second public nomination process was undertaken to solicit suggestions for members of each working group. Approximately six to ten members were chosen for each group based on their expertise and knowledge of current research related to the working group topic. Members included individuals from recently convened groups, such as the Liver Disease Subcommittee of the DDICC and NCI's GI-related Progress Review Groups, in order to complement and build upon those efforts. Due to the scientific nature of the working group reports, members were primarily researchers and healthcare providers with expertise in digestive diseases research (Appendix 2). Working group members served in an advisory role to the Commission, and each working group was led by a Chair and Vice Chair selected from among the members of the Commission.

### *A Collaborative and Inclusive Research Planning Process*

Once the full Commission was seated, it met five times and communicated extensively via conference calls and emails to conduct business in pursuit of its mission. All meetings were open to the public and advertised in advance by notification through the *Federal Register* and through the Commission's public website,<sup>3</sup> as well as by updates sent to all major digestive disease organizations. Summaries of meeting

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<sup>3</sup> The website of the National Commission on Digestive Diseases can be accessed at: <http://NCDD.niddk.nih.gov>

proceedings were also posted on the Commission website for the information of the public. Commission meetings included:

**June 12, 2006 (Arlington, VA)** – At its first meeting, the Commission received its charge from Dr. Griffin Rodgers, then Acting Director of the NIDDK, on behalf of the NIH Director, Dr. Zerhouni. The Commission members also discussed plans by the NIH to update epidemiologic data on the burden of digestive diseases in the U.S. Representatives from NIH Institutes and Centers and other Federal agencies provided an overview of digestive diseases research activities being carried out within each organization. With this background in mind, the Commission deliberated on the overall structure of the final long-range research plan and defined general issues to be addressed in each chapter. The list of chapters for the research plan and the appointment of chairs for the corresponding working groups were finalized by ongoing communication after the meeting.

**November 6, 2006 (Arlington, VA)** – The primary purpose of this meeting was to review progress reports from each working group. The chairs of each group described the major points of the background/introduction for each topic-specific chapter; the scientific scope of the chapter; areas of potential overlap with other chapters; and progress made on naming the working group members and developing material for the research plan. Commission members identified potential gaps in the proposed outline for each chapter and resolved overlap issues among chapters with related interests. In addition, Dr. Zerhouni addressed the Commission on the importance of its task in relation to the broader NIH vision for biomedical research and public health, as well as the current challenges being faced by NIH research programs.

**June 18-19, 2007 (Arlington, VA)** – This meeting focused on identifying the highest-priority research goals, objectives, and challenges, as well as major cross-cutting themes, for inclusion in the long-range research plan. It was necessary for the Commission to carefully review the many excellent research goals proposed by the working groups and determine which would potentially have the most impact on digestive diseases if pursued by the NIH. Thus, the Commission focused on developing a set of recommendations for high-priority goals that would be wide-ranging, yet manageable, in scope. Based on discussions at this meeting, working group chairs were charged with drafting a chapter for inclusion in the long-range research plan. Dr. Elizabeth Wilder, Acting Associate Director of the Office of Portfolio Analysis and Strategic Initiatives (OPASI) in the NIH Office of the Director, updated the Commission on progress and planning for the NIH Roadmap for Medical Research, which provides virtual “incubator space” for NIH programs of cross-disciplinary relevance or complexity. The Human Microbiome Project, launched in 2007, is an example of a Roadmap program that is of key importance to advancing digestive diseases research. Following the meeting, the presentation materials were posted on the Commission’s public website.

**November 19, 2007 (Rosemont, IL)** – At this meeting, Dr. Griffin Rodgers, Director of NIDDK, commended the Commission on its work to date and encouraged continued public involvement in the development and implementation of the research plan for digestive diseases. The Commission was also provided an update of progress on the development of a report on the burden of digestive diseases in the U.S. Most importantly, the Commission reviewed and discussed a draft of the entire long-range research plan for the purpose of re-organizing potential overlapping or duplicative research goals and filling in gaps in the research plan. Based on discussions at this meeting, the members made final changes to their assigned draft chapters and prepared the research plan for a public comment period. In the interim, the presentation materials from this meeting were posted on the Commission’s public website.

**May 16, 2008 (San Diego, CA)** – At its fifth and final meeting, the Commission reviewed the near-final draft research plan that incorporated suggestions submitted during the public comment period. The Commission discussed the feasibility of prioritizing its recommendations without detracting from the

inclusive nature of the research plan, which addresses multiple digestive diseases. Mechanisms or organizational structures for overseeing the implementation of the recommendations for research set forth in the plan were also considered. The Commission received an update on data developed for the report on the burden of digestive diseases in the U.S. Finally, Dr. Rodgers presented each appointed member of the Commission with a certificate signed by Dr. Zerhouni and Dr. James in recognition of their efforts over the previous 2 years. In response to discussions at this meeting, final additions and revisions were made to the recommendations for the research goals, and the Commission voted to approve the research plan in August 2008.

In addition to the public meetings of the Commission, each working group engaged in one or two conference calls to discuss and prioritize research advances, goals for future research, and major challenges and steps that would be needed to achieve the research goals. Working group members consulted informally with additional experts and colleagues from the scientific, medical, and patient communities to ensure that the final long-range research plan draws upon a broad range of perspectives and expertise. Finally, each working group had an opportunity to review and comment on a draft of the chapter for their assigned topic.

A draft of the long-range research plan was posted on the Commission's website in spring 2008 for a 30-day public comment period. Comments and suggestions received from members of the research community, patient advocacy and professional organizations, and the public at large were reviewed by the Commission and incorporated into the final research plan as appropriate before transmittal to the NIH Director and the Congress.

## **Organization of the Long-Range Research Plan**

This long-range research plan for digestive diseases is intended to be comprehensive, yet manageable, in size and scope. While acknowledging the vast number of digestive diseases and conditions that affect human health, the Commission chose an organizational structure for the research plan that categorizes diseases by common etiology, mechanism, affected organ system, or other considerations. Although there are numerous common and rare digestive diseases that have a serious impact on the daily lives and health of people throughout the Nation, it was not possible to mention every digestive disease by name in this research plan. Rather, the Commission noted that many of the recommendations are expected to have a broad impact on diseases of the digestive system, including those not explicitly mentioned. The Commission also acknowledged that many research topics or disease areas would be relevant to more than one theme within the research plan. To limit redundancy, topics were assigned to a single chapter as much as possible, with some cross-referencing where appropriate. For example, colorectal cancer research is addressed primarily in the disease-oriented chapter on "*Cancers of the Digestive System*" rather than in the organ-based chapter on "*Diseases of the Colon and Rectum*." Therefore, readers are encouraged to view this research plan in its entirety in order to locate all relevant text on a given topic.

Topic-specific areas chosen for organizing content with the long-range research plan are:

- *Research on the Basic Biology of the Digestive System*: Basic developmental biology and function of the digestive system, including growth and integrative physiology, digestion and metabolism, nutrient and fluid absorption and secretion, neurophysiology and motility, endocrinology and satiety, microbiology and microbial-host interactions, and mucosal immunology.
- *Functional Gastrointestinal Disorders and Motility Disorders*: Functional diseases for which no anatomic abnormality can be discerned and diseases associated with neuromuscular dysfunction, including irritable bowel syndrome, functional dyspepsia, gastroesophageal reflux disease (GERD), gastroparesis, chronic intestinal pseudoobstruction, and others.



- *Infections of the Gastrointestinal Tract:* Diseases caused by virulent bacteria, viruses, or other parasites that infect the digestive system, such as *E. coli*-associated diseases, cholera, *C. difficile* infection, and others.
- *Cancers of the Digestive System:* Cancers of the esophagus, stomach, pancreas, colon and rectum, and rare GI cancers.
- *Inflammatory Bowel Diseases:* Diseases associated with chronic inflammation of the GI tract, including ulcerative colitis and Crohn's disease.
- *Intestinal Failure and Regeneration, Nutritional Disorders and Support,<sup>4</sup> Surgically Modified Gut,<sup>5</sup> and Transplantation:* Conditions arising from challenges to the physical integrity of the GI tract, including short bowel syndrome, intestinal failure, intestinal transplantation, and surgically modified gut, as well as nutritional support strategies for patients with these conditions.
- *Diseases of the Oropharynx and Esophagus:* Disorders affecting the oropharynx and esophagus, including swallowing disorders (dysphagia), GERD, Barrett's esophagus, achalasia, eosinophilic esophagitis, and others.
- *Diseases of the Stomach and Small Intestine:* Disorders affecting the stomach and small intestine, including peptic ulcer disease, diarrheal diseases, celiac disease, necrotizing enterocolitis, eosinophilic GI disease, and others.
- *Diseases of the Colon and Rectum:* Disorders affecting the colon and rectum, including diverticular disease, fistulas, fecal incontinence, colonic ischemia, angiodysplasias, appendicitis, radiation proctitis, and others.
- *Diseases of the Pancreas:* Disorders affecting the pancreas, including acute and chronic pancreatitis, cystic lesions of the pancreas, and cystic fibrosis.
- *Diseases of the Liver and Biliary System<sup>6</sup>:* Disorders affecting the liver and biliary system, including viral hepatitis, fatty liver disease, drug-induced liver disease, autoimmune liver diseases, liver transplantation, liver cancer, gallstones, and others.
- *Bioengineering, Biotechnology, and Imaging:* Development of innovative techniques and state-of-the-art technologies for detection, diagnosis, and treatment of digestive diseases, including endoscopic techniques, imaging modalities, minimally invasive surgical procedures, tissue engineering and regenerative medicine, and simulation training.

Each topic-specific chapter in the long-range research plan addresses one of the major topic areas identified by the Commission and is organized along a common format with the following sections (except the chapter on "*Diseases of the Liver and Biliary System*," which presents this information in a slightly different format due to its relationship to the trans-NIH *Action Plan for Liver Disease Research*):

- *Summary of Research Goals:* Major, high-priority research goals are summarized at the beginning of each chapter.
- *Introduction and Background:* An overview of the topic, common conditions and their disease burden, epidemiology, current understanding of pathogenesis and natural history, and current means of control, cure, and/or prevention are provided.

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<sup>4</sup> The topic of nutrition was not explicitly included in the Commission's charter because research planning in this area is overseen by the existing NIH Nutrition Coordinating Committee within the Division of Nutrition Research Coordination, NIH. Nonetheless, nutritional issues and nutrition science are critically important to many digestive diseases topic areas and are addressed in the research plan as appropriate.

<sup>5</sup> Obesity, which is a major public health threat in the U.S., was not specifically chosen as an overarching topic for the Commission's research plan because it is addressed by the existing NIH Obesity Research Task Force, which released its *Strategic Plan for NIH Obesity Research* in August 2004. However, the relationship of obesity and digestive diseases is incorporated into the research plan as appropriate, for example with respect to challenges and opportunities in bariatric surgery.

<sup>6</sup> A major strategic planning effort in the area of liver and biliary system diseases was accomplished with the release of the trans-NIH *Action Plan for Liver Disease Research* in December 2004. The Commission working group assigned to this area was charged with identifying research opportunities that build on, rather than duplicate, recommendations from the *Action Plan*.

- *Recent Research Advances:* Research findings that have had a significant impact on digestive diseases research, patient health, or the ability to do future research that could benefit patients are highlighted. These advances do not represent a comprehensive survey of all progress in digestive diseases research, but are meant to indicate major, paradigm-shifting discoveries that point to new opportunities for further investigation.
- *Goals for Research:* High-impact, forward-looking, research-oriented goals are described that capitalize on new opportunities and challenges in digestive diseases research. Collectively, the research goals in each chapter represent those identified by the Commission as the highest-priority aims to be achieved in digestive diseases research over the next 10 years. The goals are numbered solely for ease of future reference and are not listed in priority order. Each goal includes a short list of specific objectives that represent more discrete, shorter-term steps toward achieving the overall goal.
- *Major Challenges and Steps To Achieve the Research Goals:* Barriers to conducting research and to achieving the group of goals for each topic area are described. In addition, this section identifies important steps that, if taken, would help overcome these barriers and accelerate progress toward realizing the research goals.

Finally, the Commission's research plan concludes with a summary of common themes and steps for implementation that were identified by multiple working groups as important research goals and challenges. These common themes are broadly applicable to many digestive diseases or questions in basic biology of the digestive system. In particular, the Commission recognized the fundamental importance of finding ways to achieve and sustain a robust pipeline of trained investigators with knowledge of and a commitment to digestive diseases research. Many topic-specific chapters identify specialized areas of research training or recruitment that would help to sustain the investigator pool in specific fields of research. In addition, a working group of Commission members developed goals and recommendations for research training, education, and the recruitment of new investigators to digestive diseases research; these recommendations are described in the *Conclusion: Common Themes and Steps for Implementation* chapter.

The steps proposed to aid in implementation of the research address current gaps in scientific knowledge and critical opportunities for NIH research and training efforts over the next decade that have the potential to impact multiple areas of digestive diseases research. Pursuing these opportunities will allow the NIH and the research community to find innovative solutions to reduce the toll that digestive diseases take on the health and quality of life of individuals throughout this Nation.